

# frontotemporal syndromes in ALS

Jim Howe





W. B. Yeats, 1865-1939

Education is lighting a fire, not  
filling a bucket



All hope abandon, ye who enter here.  
*Canto III., line 9.*

Incurable but not untreatable!

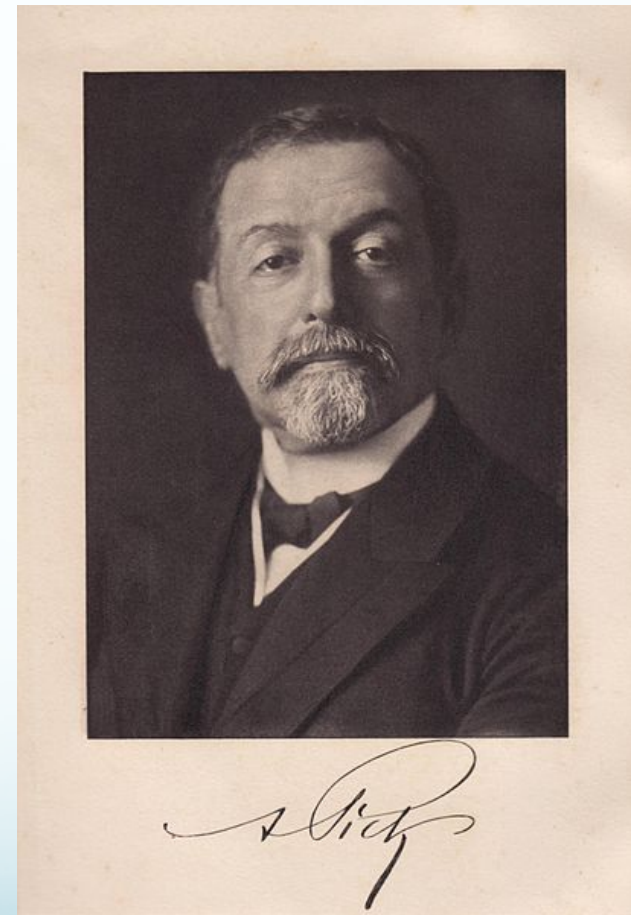
# Amyotrophic Lateral Sclerosis (MND)

- Charcot & Joffroy (1869)
- Dornbüth (1889)
- Marie (1892)
  - oOoOoOo
- Furukawa (1959)
- Hudson (1981) review of cases from 1955-'80: 15% F-ALS, 22% sporadic
- Neary (2000) [Lund & Manchester:FTD (1994)]



# frontotemporal dementia

- 1904: progressive loss of language & behaviour change clearly described, noted left brain atrophy
- 1911: histology described by Alzheimer; “Pick Bodies” ‘Pick Cells” & focal atrophy
- 1982: Mesulam PPA
- 1986 to 1994: Manchester & Lund teams; FTD, clinical & pathological





# “psychological” problems in ALS

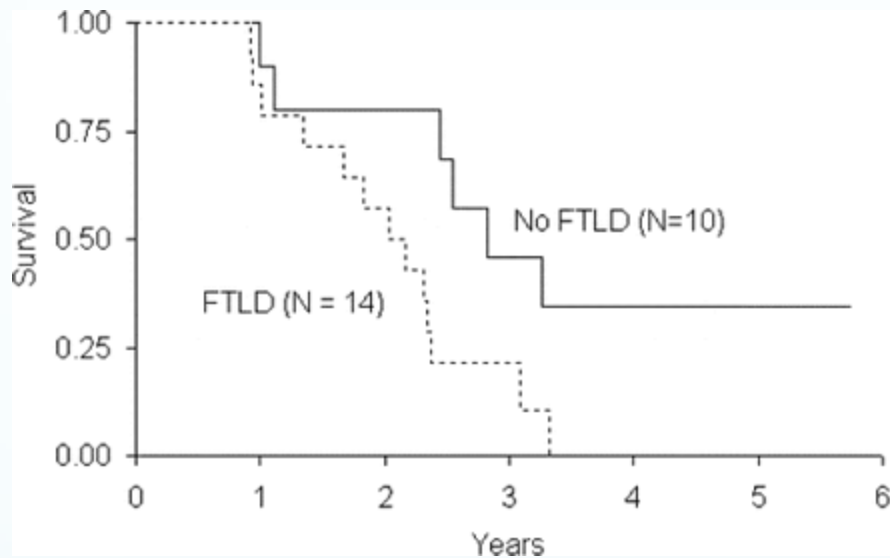
- anger, loss, guilt, anxiety, depression, somatisation,
- frontotemporal syndromes
  - not severe enough to disrupt social life etc.
  - Pseudo Bulbar Affect
- Fronto-Temporal Dementia
- neuro-muscular respiratory failure: fatigue, clouding, delirium
- Atherothromboembolism, diffuse white matter ischaemia
- Alzheimer’s Disease, HD
- other medical problems eg liver failure, alcoholism

# why pay attention?

- prognosis: shorter with FTD
- care:
  - communication more difficult
  - decision making more difficult
    - risks, benefits & BURDENS of interventions: PEG, NIV
  - psychological distress
  - carer stress & distress
- research:
  - trial design
  - care: techniques, systems

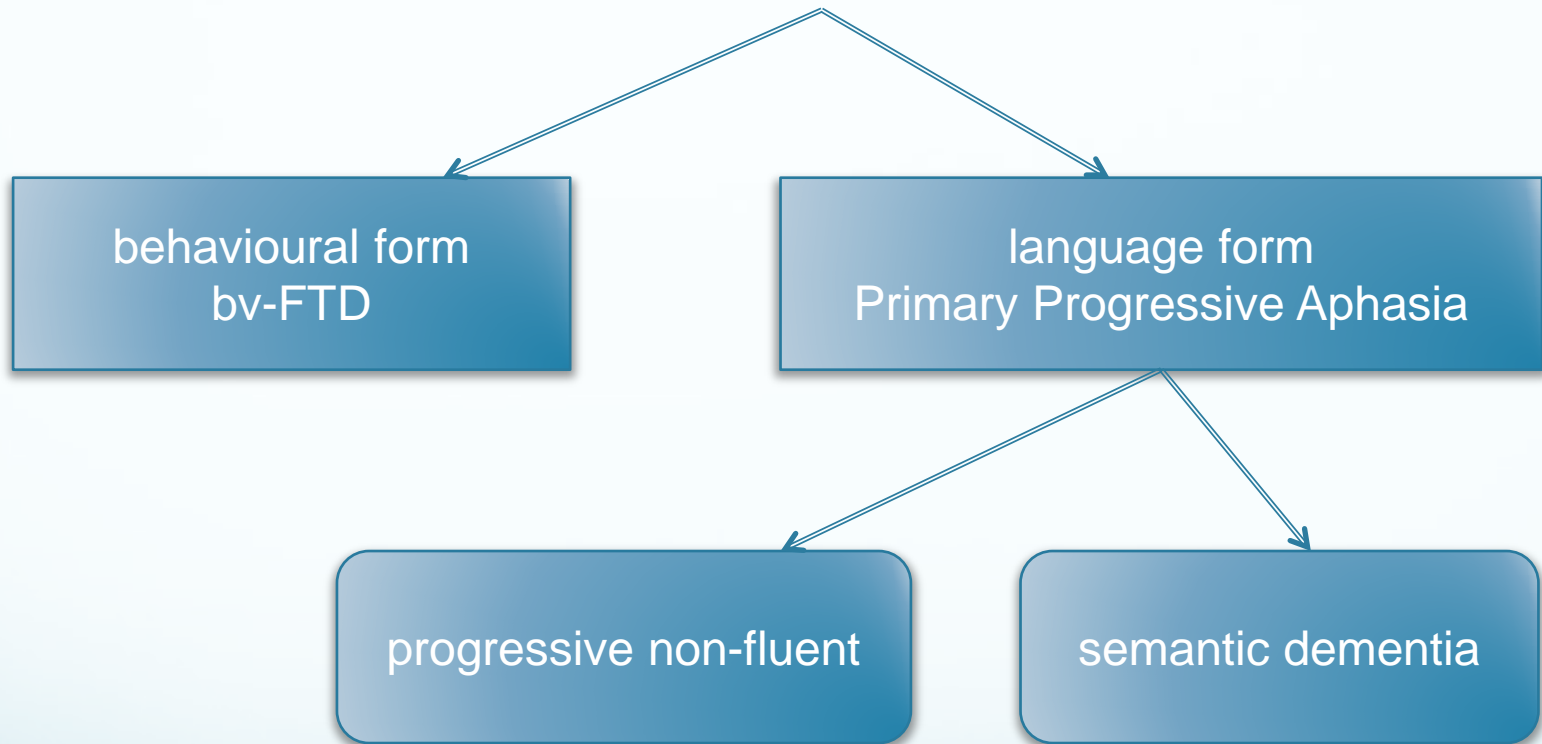
Figure 1: NIV Delivered through BIPAP Synchrony via Full Face Mask





*Figure. Kaplan-Meier survival estimates for 24 patients with ALS with bulbar onset of disease by presence or absence of frontotemporal lobe dementia (FTLD). Log-rank test for equality of survival functions,  $p = 0.038$ .*

# FTD





# bvFTD -progressive

1. behavioural disinhibition:
  1. socially inappropriate
  2. loss of manners
  3. impulsive, careless, rash
2. Apathy, inertia
3. loss of sympathy, empathy
  1. less response to others
  2. less social interest, personal warmth
4. perseverative, stereotyped, compulsive/ritualistic
  1. simple movements
  2. complex behaviours
5. hyperorality, dietary changes
  1. food preferences, fads
  2. binge eating, alcohol, cigarettes
  3. oral exploration, inedibles
6. neuropsych. profile:
  1. executive deficits, Trails-B, letter fluency, errors
  2. relative sparing of episodic memory
  3. relative sparing of visuospatial skills



# & ALS?

## FT Dementia

- clearly begin together
- PPA or bvFTD with early emergence of ALS features
- ALS with emergence of FTD features, quickly becoming full syndrome

## FT Syndrome

- pwALS:
  - gradual emergence of SOME features
    - verbal fluency, especially action verbs, progress to dysphasia
    - empathy/sympathy, progress to uncaring selfcentredness
    - rigidity, progress to anger/despair if strict care process not followed

# subtypes of FTS in ALS

Strong et al 2009

ALS

A pure motor system disorder as defined by the El Escorial criteria with no clinical evidence of non-motor system involvement

FTD

criteria for FTD fulfilled

ALSbi

Predominant behavioural dysfunction

ALSsci

Deficits in one or more of verbal and design fluency, verbal reasoning, visual attention, initiation of random movements, and problem solving, includes disturbances in executive function; insufficient to meet the Neary criteria for FTD

June 10-13, 2007  
London Ontario Canada



# ALS –FTD?

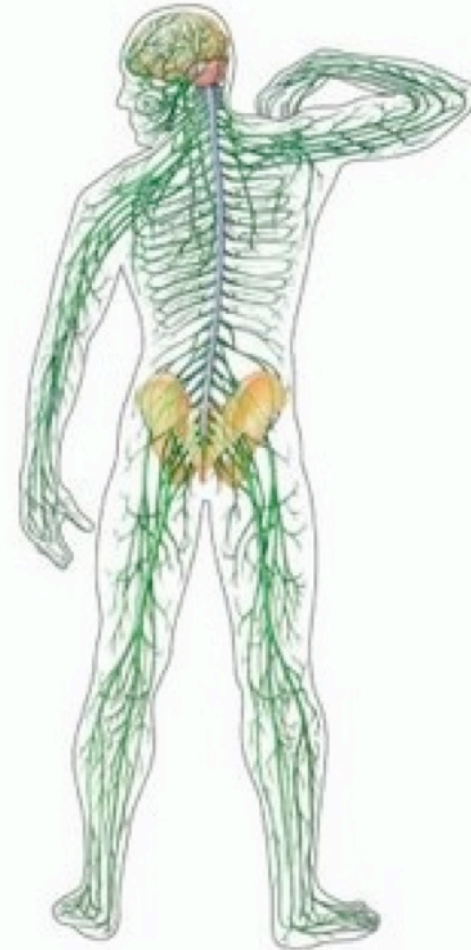
- reports suggest up to 20%, full syndrome
- ‘milder forms’ up to 40%
- PBA 50% -?
- behaviour changes, e.g. restless, apathy, rigidity, disinhibited 63% of ALS
- literature struggling with how to understand & explain all this, & label different presentations, molecular biology & genetics advancing too

# overlap syndromes?

- coincidence
- share risk factors
- interaction between pathological factors
- different presenting phenotypes of the same disease  
e.g. juvenile v adult onset HD

# Ravits 2009

- focality & spread in ALS
  - (see also Braak staging in PD)
- ALS always focal onset, trigger event
- contiguous spread along the 3D anatomy of CNS
  - active process, linear & orderly
  - kinetic factors? protective factors? determine progression
- applies to frontal & temporal lobes too



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NUMBER 10

## **Long-term neurological conditions: management at the interface between neurology, rehabilitation and palliative care**

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# problems –frontal D or synd.

- executive: changing roles, finances, will, PoA, early planning for interventions, EoL care choices
- apathy, fatigue, depression ???
- irritability, poor judgment & impulsivity, rigidity/compulsive behaviours
- loss of insight – compliance/cooperation
- loss of empathy, self-centeredness, no appreciation
- PBA
- social disinhibition, aggression
- hyperorality, and poor swallow!

# problems -language

- communication!!!!
  - physical:
    - dysarthria, dysphonia, quiet voice -  
diaphragm weakness! hand weakness
  - cortical:
    - dysphasia, speech apraxia, PBA
    - rigidity
    - perseveration
    - loss of insight
    - executive problems with communication devices

# Pseudobulbar affect

- Common: ALS, PSP, MSA, MS, stroke
- Distressing
- Social limitation, isolation
- Explanation, relaxation
- Drugs:
  - SSRI's,
  - dextromethorphan + quinidine



# strategies for care

- environmental: PoA, car keys, power chair, food, call button, alarms, regulate visitor/activities
- behavioural: avoid, reward, distract, relaxation training, communication skills
- pharmacological: SSRI's, benzo's, ?amphetamine, dextromethorphan, dopamine antagonists, analgesics, morphine
- physical: communication aids, comfort-eg tilt 'n space
- internal to carer: reactions and responses, supports

(also see ABI literature)



# what can we do?

- Promote use of consistent terminology!!
- Refer to “cognitive / behaviour” changes unless a formal diagnoses of FTD is available.
- Acknowledge that frontotemporal syndromes are more common in MND than previously thought.
- Promote awareness of the non-motor symptoms without increasing the FEAR FACTOR around “dementia”

references:

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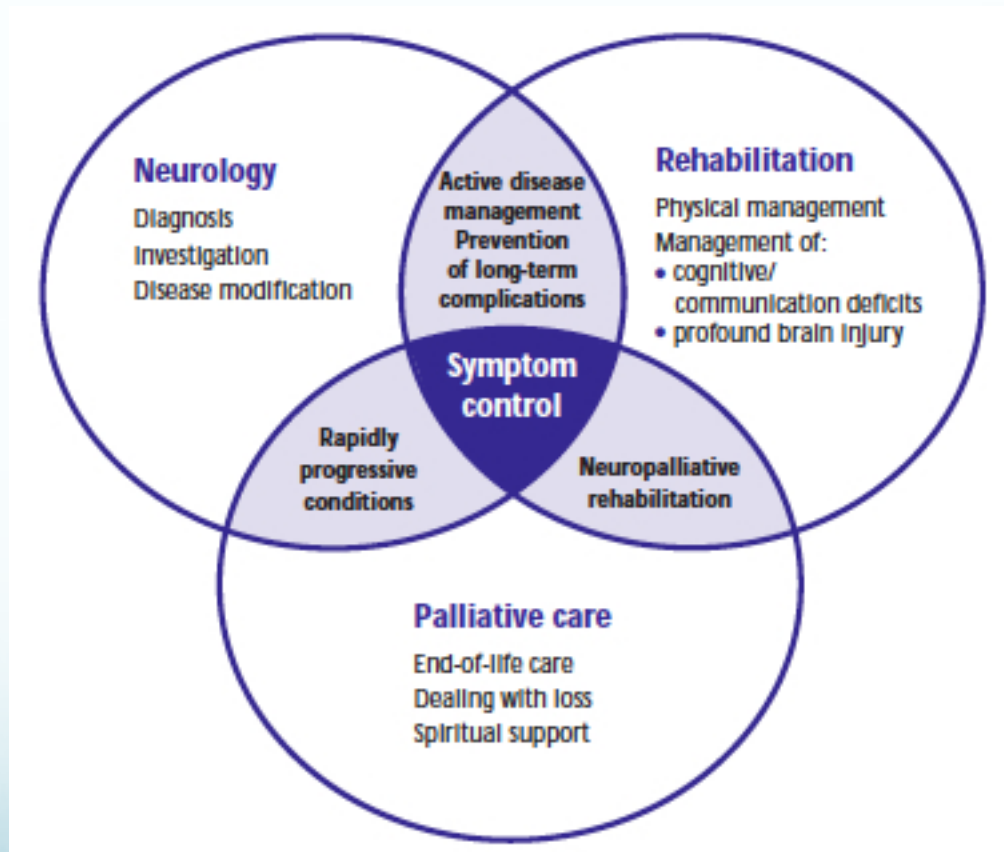
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Deconstructing motor neuron degeneration

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Rosen H *Drugs Today* 2008;44:661  
Dextromethorphan/quinidine sulfate for pseudobulbar affect

# neuropalliative rehabilitation



# neuropalliative rehabilitation

